대한심장학회 THE KOREAN SOCIETY OF CARDIOLOGY 심장학연구재단 THE KOREAN CARDIAC RESEARCH FOUNDATION

ALL FOR HEART HEART FOR ALL

KSC

# 2019 Daily

The 63rd Annual Scientific Meeting of The Korean Society of Cardiology

**2019. 10. 18 (Friday)**

## Today's Highlights

**New Frontiers in Cardiology 1**
*Plenary Lecture in Future Medicine*
08:40-10:10 AM / Rm. Theatre

**Heart Failure 1**
*Essence of Recent HF Trials*
08:40-10:10 AM / Rm. Cosmos

**Cross Specialty: Nephrology & Cardiology**
*What Nephrologists Want to Say to Cardiologists*
10:20-11:50 AM / Rm. Theatre

**Featured Clinical Research 1**
14:00-15:30 PM / Rm. Theatre

**Cross Specialty: Arrhythmia & Heart Failure**
15:40-17:10 PM / Rm. Theatre

**Intervention 2**
*The Interventional Cardiovascular Medicine Perspective: Insights, Innovation, and the Next Decade*
15:40-17:10 PM / Rm. Walker 2

**Echocardiography 2**
*Valvular Heart Diseases*
15:40-17:10 PM / Rm. Art

## Welcome Message

***You Ho Kim, MD, PhD***
*Chairperson, The Korean Society of Cardiology*

*"We are pleased to announce the opening of the 63rd Annual Scientific Meeting of the Korean Society of Cardiology (KSC 2019) in Seoul, Korea."*

On behalf of the Korean Society of Cardiology (KSC), a scientific society representing knowledge, prevention and treatment in cardiology, I am pleased to announce the opening of the 63rd Annual Scientific Meeting of the Korean Society of Cardiology (KSC 2019), which will be held on October 18-20, 2019, at the Grand Walkerhill in Seoul, Korea.

KSC was established in 1957 as one of the principal national societies of cardiology in Korea and has been offering countless cardiology conferences, symposiums and educational lectures. As the increase of chronic cardiovascular diseases has become a significant social issue, it is fundamental for cardiologists to keep abreast of current knowledge by participating at KSC 2019.

I welcome all the scientists, health professionals, educators, and those working for the advancement of cardiology and promoting the importance of cardiovascular diseases related research. I also look forward to our young cardiologists to learn more about cardiovascular diseases that advance our medical and technological needs at KSC 2019.

Autumn is a second spring when every leaf is a flower. Wish you the warmth and joy in this wonderful season while enjoying our meeting.

***Kee Sik Kim, MD, PhD***
*President and CEO, The Korean Society of Cardiology*

*"The 63rd Annual Scientific Meeting of the Korean Society of Cardiology (KSC 2019) is going to be a valuable opportunity to share the knowledge on how to deal with cardiovascular diseases and help more people suffering from heart diseases."*

I am pleased to send warm greetings to all those participating in the 63rd Annual Scientific Meeting of the Korean Society of Cardiology (KSC 2019). This meeting is going to be a valuable chance to share the knowledge on how to deal with cardiovascular diseases and help more people suffering from heart diseases.

Advances in cardiology have provided hope to millions of people who suffer from cardiac issues and disorders, including hypertension, coronary artery disease, heart attack, stroke and heart failure.

With regard to the advances in cardiology, KSC aims at improving human health in general and contributing to the treatment and prevention of cardiovascular diseases. Thus far, KSC has contributed significantly to the national cardiovascular development by providing basic and clinical research knowledge. As we have been endeavoring to acquire expert cardiovascular knowledge and present outstanding achievements to the international societies, we have also been developing quantitatively as well as qualitatively with the members who have strived in medical treatment and research. I appreciate the members of KSC and all those dedicated in the cardiac field for their efforts and truly welcome their attention and participation at KSC 2019.

# Program at a glance: Day 1, Oct 18, 2019

| | Theatre Main Arena (B1) | Grand 4 (B1) | Walker 1 (1F) | Walker 2 (1F) | Cosmos (3F) | Calla (3F) | Art (4F) | Pine (4F) | Oak (4F) | Grand Hall (B1) Abstract / Case Zone 1 | Grand Hall (B1) Abstract / Case Zone 2 | Vista Hall (B2) Abstract / Case Zone 3 | Vista Hall (B2) Abstract / Case Zone 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 08:40 - 10:10 | **New Froniters in Cardiology 1** Plenary Lecture in Future Medicine | **Lipid 1** Lessons Learned from Recent CV Outcome Clinical Trials Using Cardiometabolic Drugs | **Arrhythmia 1** ECG Review Course | **Myocardial Infarction 1** Joint Collaboration for Asian AMI Guideline | **Heart Failure 1** Essence of Recent HF Trials | **Basic Research 1** Recent Updates in Basic Cardiovascular Research | **Cardiometabolic Syndrome 1** Hot Topic in Cardiometabolic Syndrome 1 | **Imaging 1** Multimodal Imaging Approach for Heart Failure | | **CAD 1** 1-8 | | **Hypertension 1** 9-16 | **Arrhythmia 1** 17-25 |
| 10:20 - 11:50 | **Cross Specialty: Nephrology & Cardiology** What Nephrologists Want to Say to Cardiologists | **Lipid 2** Overview and Deep-dive Discussion: Recent Lipid Guidelines | **Arrhythmia 2** AF Screening and Stroke Prevention | **Myocardial Infarction 2** Cardiogenic Shock: Are We Ready for Changing the Approach? | **Heart Failure 2** Cardiac Critical Care - Case Based Approach | **Basic Research 2** Tissue Engineering Technology Using Stem Cells for Cardiovascular Disease | **Cardiometabolic Syndrome 2** Hot Topic in Cardiometabolic Syndrome 2 | **Imaging 2** Multimodal Imaging Approach for Structural Heart Disease Intervention | | **Echocardio-graphy 1** 26-33 | **Intervention 1** 34-40 | **Hypertension 2** 41-48 | **Arrhythmia 2** 49-57 |
| 12:00 - 12:40 | **Scientific Session [Bayer]** | | **Diamond Session [Pfizer/BMS]** | **Scientific Session [Samjin]** | **Scientific Session [Boryung]** | | **Healthcare Policy: Special Lecture** Comprehensive Cardiac Rehabilitation | | | E-Poster 1-83 | | | |
| 12:40 - 14:00 | | | | | | | | | | Case Presentation: **AMI & CAD 1** 1-7 | Case Presentation: **Intervention 1** 24-30 | Case Presentation: **Pediatric Cardiology** 16-23 | Case Presentation: **Heart Failure** 8-15 |
| | | | | | | | | | | Moderated Poster Presentation: **Basic Research** 1-5 | Moderated Poster Presentation: **CAD 1** 6-15 | Moderated Poster Presentation: **Vascular+ Hypertension** 16-22 | Moderated Poster Presentation: **Echocardio-graphy+Imaging** 23-32 |
| 14:00 - 15:30 | **Featured Clinical Research 1** | **Women Heart Disease 1** Exercise in Women | **Myocardial Infarction 3** AMI Updates and Debates | **Intervention 1** New Corner of Invasive Coronary Physiology in 2019 | **Smart Health** 의료정보화와 심장질환 | **JCS[1]-KSC Joint Session: Basic Research** Roadmap for Cardiac Regeneration | **Echocardio-graphy 1** Reviewing the Old and Learning the New in Heart Failure | **VNHA[2]-KSC Joint Session: CHD** Past and Present in Congenital Heart Disease – Vietnam and Korea | **Imaging 1** 58-65 | **CAD 2** 66-73 | **Heart Failure 1** 74-81 | | |
| 15:40 - 17:10 | **Cross Specialty: Arrhythmia & Heart Failure** 1. What You May Not Know... 2. The Good, the Bad, and the Weird | **Women Heart Disease 2** Arrhythmia in Women | **Meet the Editor** Why I Chose This Paper from Korea | **Intervention 2** The Interventional Cardiovascular Medicine Perspective: Insights, Innovation, and the Next Decade | **Cardiac Pathology** Cardiac Pathology Services and Education | **IHA[3]-KSC Joint Session: Echocardio-graphy/Imaging** Imaging Issues of HCM and ACHD | **Echocardio-graphy 2** Valvular Heart Diseases | **KCDC[4]-KSC Joint Session: CHD** Cardiovascular Disease Registry | **Imaging 2** 82-89 | **Echocardio-graphy 2** 90-97 | **Intervention 2** 98-105 | **Lipid** 106-113 | **Arrhythmia 3** 114-122 |

1) JCS: Japanese Circulation Society 2) VNHA: Vietnam National Heart Association 3) IHA: Indonesia Heart Association 4) KCDC: Korea Centers for Disease Control & Prevention

## Scientific & Diamond Sessions

### Scientific Session 1 [Bayer]

The Bigger Picture in Stroke Risk Reduction and Anticoagulation

›› Oct 18, 12:00-12:40 PM Rm. Theatre

### Scientific Session 2 [Samjin]

Strategy for Prevention of Cardiovascular Event

›› Oct 18, 12:00-12:40 PM Rm. Walker 2

### Scientific Session 3 [Boryung]

Current Issues in the Management of Hypertension in Korea

›› Oct 18, 12:00-12:40 PM Rm. Cosmos

### Diamond Session [Pfizer/BMS]

Strategies to Optimize Management of CVD

›› Oct 18, 12:00-12:40 PM Rm. Walker 1



# Arrhythmia

## Rationale of AF Screening to Prevent Stroke

***Ben Freedman, MD, PhD***
*University of Sydney, Australia*

Atrial fibrillation (AF) is often asymptomatic and undetected in older people, so if screening for unknown AF was carried out at scale, and people found were treated with oral anticoagulant, many strokes could be prevented.

Meta-analysis and systematic reviews of screening studies for AF by Lowres, et al. have shown that unknown AF increases dramatically with age and is more common in males. Over the age of 65, the detection rate is 1.4% on a single timepoint screen with either pulse taking or electrocardiogram (ECG), but for the age group between 80 to 84, it is 1.9%. The combination of screening detection rate and risk of stroke over the age of 65 has led a number of continental and country-specific guidelines to recommend screening in patients over that age, but this is not practiced worldwide.

***Screening tools***

The method of single timepoint screening varies from physical examination using pulse palpation or auscultation of the heart, or Korotkoff sounds while measuring blood pressure, to a handheld ECG single lead rhythm strip, and a conventional ECG. Single timepoint screening will largely detect persistent or very high burden paroxysmal AF, and will therefore miss a lot of paroxysmal AF, causing underestimation of unknown AF. To overcome this issue, a number of more intense screening protocols have been adopted.

***New approaches and consumer-led screening***

There are now many devices available to both physicians and the general population which can screen for AF, from photoplethysmographic (PPG) devices in smartphones, smartwatches and fitness trackers and rings. They can also be used semi-continuously, and may therefore detect AF with low risk, as with implanted devices, so we will need to pay much greater attention to the health impact of what is now being promoted to consumers.

## Non Pharmacological Management of AF (Weight Loss, Hypertension Control, Etc); Focused on Upstream Therapies

***Yong-Soo Baek, MD***
*Inha University Hospital, Korea*

Atrial fibrillation (AF) is often, but not always, associated with systemic illness and risk factors, such as obesity, sleep apnea, hypertension, smoking, excessive exercise or alcohol. At the atrial level, AF is characterized by atrial remodeling as a result of electrical, metabolic, autonomous, and structural changes (fibrosis, inflammation, hypertrophy, and oxidative stress). Increasing evidence supports the concept of "upstream" therapy in the management of AF (**Figure 1**). Downstream therapy as rhythm control therapy directly targets triggered activity, action potential duration shortening and slowed conduction across the atria.

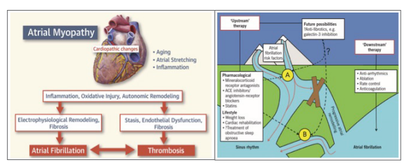



**Figure 1.** Upstream and downstream therapies

Some previous studies demonstrated the beneficial effects of long-term sustained weight loss and participation in a tailored exercise program on reducing AF recurrence in the obese population. Interventions to decrease obesity may reduce the population burden of AF. In another study, even in healthy Asian populations without comorbidities, prehypertension and impaired fasting blood glucose were important risk factors of AF. Combined upstream and downstream therapy may offer a double lock to slow progression of AF, but more work needs to be done.

**Arrhythmia 2**
**AF Screening and Stroke Prevention**
›› Friday, Oct 18, 10:20-11:50 AM / Walker 1

# VNHA-KSC Joint Session: CHD

## Surgical Treatment for CHD in Vietnam

***Nguyen Ly Thinh Truong, MD, PhD***
*National Children's Hospital, Vietnam*

Heart surgery for congenital heart disease (CHD) began in Vietnam during the 1970s at Viet Duc Hospital, which was during the Vietnam War. First successfully-operated case report was a patient with patent ductus arteriosus (PDA) ligation, followed by pulmonary valvotomy for critical pulmonary stenosis (PS). Since 1990, Carpentier Heart Institute in HoChiMinh city successfully performed open heart surgeries for children with CHD. The majority were simple lesions, including atrial septal defect (ASD), ventricular septal defect (VSD) and tetralogy of fallot (TOF).

Together with improvement of economic condition, the surgical treatment for CHD has been widespread among many centers throughout the country. Now there are up to 18 centers which can perform open heart surgery for children from North to South of Vietnam. The number of CHD surgeries performed has not been accurately recorded, but it is estimated that approximately 4,500 to 5,000 cases are performed each year in a population of 96 million people. Currently, the quality of treatment for simple lesion is comparable among institutions, and outcomes are good with the mortality rate less than 5% in ASD and VSD patients. However, there are challenges for complex open heart surgery and different outcomes are reported. Neonatal open heart surgery can be performed in a few centers (5 centers in the whole country) and is still a challenge for most of the centers. Biventricular repair during neonatal period can be successfully performed in 2 or 3 centers, but single ventricle palliation still remains a challenge for all centers.

Currently, only one center, which is dedicated for neonatal open heart surgery, is able to perform the Norwood operation with an acceptable mortality. Despite the quality of CHD screening program has much improved, there are a lot of neonate and infant patients born with critical CHD who die before diagnosis. Other remaining issue is adult CHD, which is likely to become a heavy burden for the healthcare system in the near future.

The progress of surgical treatment for CHD in Vietnam showed a dramatic improvement in the past two and a half decades. However, a lot of difficulties and challenges in the near future are expected, which will require a strong support and collaboration from the developed countries to overcome the issues.

## Surgical Treatment for TOF in Infant and Adult

***Chang-Ha Lee, MD, PhD***
*Sejong Hospital, Korea*

Surgical outcomes of tetralogy of fallot (TOF) repair have been improving with excellent outcomes in early mortality and morbidity. Also, long-term survival after repair continues to improve. However, several issues still need to be addressed, such as optimal treatment in small symptomatic patients, how to preserve pulmonary valve function, and optimal timing of pulmonary valve replacement (PVR) in patients suffering from pulmonary regurgitation (PR) after repair.

For symptomatic neonates or young infants, surgical options include early primary repair or aortopulmonary shunting followed by repair. These two options have their advantages and disadvantages, and their outcomes have been reported to be well-acceptable. Still, one topic, which is the possibility of an aortopulmonary shunt preserving the pulmonary valve annulus in TOF with pulmonary stenosis, remains to be confirmed.

Post-repair PR is not a benign sequelae and contributes to right ventricular (RV) dilatation and dysfunction, left ventricular (LV) dysfunction, and electromechanical dyssynchrony. Therefore, every effort should be made to prevent PR during the repair. Even in patients with small pulmonary valve annulus, intraoperative pulmonary valve ballooning has been applied to obtain the optimal valve function.

The last issue is about the optimal timing of PVR in patients with severe PR. Recently, 2018 AHA/ACC guidelines for the management of adults with congenital heart disease (CHD) recommend to consider PVR in symptomatic patients and patients without symptoms but showing ventricle systolic dysfunction, severe RV dilatation, RV outflow tract obstruction, and progressive reduction in exercise tolerance. In addition, PVR should be indicated in cases of sustained tachyarrhythmia and residual lesions requiring surgical interventions.

**VNHA-KSC Joint Session: CHD**
**Past and Present in Congenital Heart Disease – Vietnam and Korea**
›› Friday, Oct 18, 14:00-15:30 PM / Pine

# Heart Failure

## PARAGON-HF

*Ju-Hee Lee, MD*
*Chungbuk National University Hospital, Korea*

Currently, there is no approved treatment for heart failure (HF) with preserved ejection fraction (HFpEF). No medication has reduced mortality in such patients, although prior trials have pointed toward some important clinical benefits. In this session, Dr. Ju-Hee Lee will present the results of the recently released global phase III PARAGON-HF study, investigating the safety and efficacy of sacubitril/valsartan versus the active comparator valsartan in HFpEF patients. Currently, sacubitril/valsartan (approved as Entresto® since 2015) is an essential treatment in patients with HF with reduced HFrEF, based on its superiority to the angiotensin-converting enzyme (ACE) inhibitor enalapril and its ability to significantly reduce cardiovascular (CV) death and HF hospitalizations.

PARAGON-HF is the largest clinical trial in HFpEF conducted to date. This phase III randomized, double-blind, parallel group, active-controlled, 2-arm, event-driven trial compared the long-term efficacy and safety of sacubitril/valsartan versus valsartan in 4,822 patients with HFpEF (EF ≥45%, elevated natriuretic peptides, structural heart disease, New York Heart Association [NYHA] functional class II to IV). The primary endpoint of the trial was the composite of total (first and recurrent) HF hospitalizations and CV death. Sacubitril/valsartan reduced the composite primary endpoint of total HF hospitalizations and CV death by 13 percent over an average of about 3 years, but the difference missed statistical significance (RR=0.870; 95% CI: 0.753, 1.005; p=0.059). The result was primarily driven by a nearly 15 percent reduction (p=0.056) in total HF hospitalizations (first and recurrent). Secondary endpoint analyses, exploratory in nature, showed that sacubitril/valsartan patients experienced less worsening in quality of life than valsartan patients based on KCCQ Clinical Summary Score (CSS) at 8 months. Change in the NYHA functional class was also more favorable in the sacubitril/valsartan group than in the valsartan group. Additionally, treatment with sacubitril/valsartan resulted in a significant reduction in the risk of the composite renal endpoint. No difference in all-cause mortality was observed between the two groups. Pre-specified subgroup analyses suggested even greater effects in individuals with a left ventricular EF equal to or below the median of 57% (22 percent reduction in primary endpoint; 95% CI: 0.641, 0.949) and in women (27.5 percent reduction in primary endpoint; 95% CI: 0.588, 0.895). Safety and tolerability were consistent with previously reported sacubitril/valsartan data (**Figure 1**).

| Outcome | Sacubitril-Valsartan (N=2407) | Valsartan (N=2389) | Ratio or Difference (95% CI) |
|---|---|---|---|
| **Primary composite outcome and components** | | | |
| **Total hospitalizations for heart failure and death from cardiovascular causes†** | | | RR, 0.87 (0.75–1.01) |
| Total no. of events | 894 | 1009 | |
| Rate per 100 patient-yr | 12.8 | 14.6 | |
| Total no. of hospitalizations for heart failure | 690 | 797 | RR, 0.85 (0.72–1.00) |
| **Death from cardiovascular causes — no. (%)** | **204 (8.5)** | **212 (8.9)** | **HR, 0.95 (0.79–1.16)** |
| **Secondary outcomes** | | | |
| **Change in NYHA class from baseline to 8 mo — no./total no. (%)** | | | OR, 1.45 (1.13–1.86) |
| Improved | 347/2316 (15.0) | 289/2302 (12.6) | |
| Unchanged | 1767/2316 (76.3) | 1792/2302 (77.8) | |
| Worsened | 202/2316 (8.7) | 221/2302 (9.6) | |
| **Change in KCCQ clinical summary score at 8 mo‡** | **−1.6±0.4** | **−2.6±0.4** | **Difference, 1.0 (0.0–2.1)** |
| Renal composite outcome — no. (%)§ | 33 (1.4) | 64 (2.7) | HR, 0.50 (0.33–0.77) |
| **Death from any cause — no. (%)** | **342 (14.2)** | **349 (14.6)** | **HR, 0.97 (0.84–1.13)** |

**Figure 1.** Primary and secondary outcomes of PARAGON-HF (Adapted from N Eng J Med 2019; DOI: 10.1056/NEJMoa1908655)

Although this trial missed statistical significance for the primary endpoint, the evidence from the trial, including improvement in various measures of symptoms, quality of life, and renal function, suggest that treatment with sacubitril/valsartan may result in clinically important benefits in HFpEF patients.

**Heart Failure 1**
**Essence of Recent HF Trials**
›› Friday, Oct 18, 08:40-10:10 AM / Cosmos

# IHA-KSC Joint Session: Echocardiography/Imaging

## Congenital Heart Disease Imaging Trend: Are We Already Moving Toward the Use of Non-invasive Technique?

*Oktavia Lilyasari, MD*
*National Heart Center Harapan Kita Hospital, Indonesia*

Congenital heart disease (CHD) occurs in about 6 to 8 out of 1,000 live births with the increasing prevalence and can be attributed to major improvements in diagnosis. Imaging is fundamental in the diagnosis of CHD. It outlines the anatomy and physiology, helps to refine management, evaluates the consequences of interventions and helps guide prognosis. The choice of imaging modality has thus become an important issue. However, no single available imaging modality fulfills all these roles. Therefore, assessment for CHD must involve a variety of modalities that can be used in a complementary fashion, and that together are sensitive, accurate, reproducible, and cost effective, whilst minimizing harm.

Transthoracic echocardiography examination (TTE) which has been the first modality has a few limitations. In previous years, the diagnosis and the treatment of CHD have often depended on cardiac catheterization. In many institutions, it still remains the gold standard against which other modalities are used.

The state-of-the-art multi-slice computed tomography (MSCT) imaging techniques for CHD are useful to evaluate diverse cardiovascular and airway abnormalities with improved accuracy, patient and user-friendliness. Therefore, MSCT is steadily becoming an invaluable imaging modality to fill the gap among echocardiography, cardiac catheterization and cardiac magnetic resonance imaging (MRI). Currently, cardiac MRI has been demonstrated to be an adequate technique to evaluate several important aspects of ventricular function, intra-cardiac flow dynamics, including valve regurgitation and stenosis, and large vessel flow. Furthermore, it has proven to be an important technique in the anatomical characterization of complex CHD, particularly of the venous connections, atrial arrangement, and ventricular-great arteries relationship.

## Recent Issues in ACHD: Focused on Treatment Decision

*Youngmin Eun, MD, PhD*
*Yonsei University Gangnam Severance Hospital, Korea*

The number of patients with adult congenital heart disease (ACHD) continues to grow. As a result of major achievements in pediatric cardiac care, however, a dramatically increasing number of patients with congenital heart disease (CHD) are flourishing well into adulthood. This heterogeneous and aging population of ACHD patients, many of whom represent the first generation of middle-age survivors, faces unique health care issues and challenges.

As a field, ACHD has evolved markedly during the past decade on several fronts, including imaging, arrhythmia management, percutaneous interventions, surgical techniques, research, and multidisciplinary care that extend beyond the cardiac realm. These patients require specialized care and there are few cardiologists and surgeons, as well as other subspecialists (e.g., anesthesia, hepatology, nephrology, neurology, etc.) with training who are comfortable in the management of ACHD patient population.

In addition, ACHD patients may have complex psychosocial issues. A comprehensive multidisciplinary team approach can best address the management for all of these issues. Regional centers of excellence for ACHD care with congenitally-trained cardiac surgeons, cardiologists, and other medical subspecialists are required to make a decision and optimize their treatment for better lifelong outcomes.

**IHA-KSC Joint Session: Echocardiography/Imaging**
**Imaging Issues of HCM and ACHD**
›› Friday, Oct 18, 15:40-17:10 PM / Calla



# Healthcare Policy: Special Lecture

## Comprehensive Cardiac Rehabilitation: Opportunities and Challenges!

*Peter H. Brubaker, PhD*
*Wake Forest University, USA*

Cardiac rehabilitation (CR) has evolved over the past decades from simple monitoring for the safe return to physical activities to a multidisciplinary approach that focuses on patient education, individually tailored exercise training, modification of the risk factors and the overall well-being of the cardiac patients (**Figure 1**). Recent research has demonstrated that tremendous benefits can be derived from the optimal use of cardiac rehabilitation in patients with various cardiac pathologies, including ischemic heart disease, heart failure (HF) and post-heart surgery. The benefits of cardiac rehabilitation include mortality and morbidity reduction, symptom relief, reduction in smoking, improved exercise tolerance, risk factor modification, and the overall psychosocial well-being. Unfortunately, CR remains considerably underutilized mainly because of referral barriers and poor enrollment/

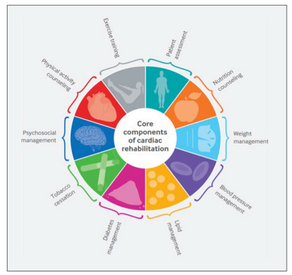



**Figure 1.** Components of cardiac rehabilitation

uptake. Unfortunately, only 14% of myocardial infarction (MI) and 31% of coronary artery bypass graft (CABG) patients participate in CR. Future studies should focus on how to include more cardiac patients in CR. For instance, the Centers for Disease Control and Medicare have teamed up to expand CR participation as part of the "Million Hearts" program. Clearly, greater efforts are needed to overcome the social, economic, and practice behaviors for referral, enrollment, and adherence to CR such that the clinical benefits can be attained. In terms of

*Continued on page 5*

# Myocardial Infarction

## Updated JCS 2018 guideline on Diagnosis and Treatment of Acute Coronary Syndrome

*Satoshi Yasuda, MD, PhD*
*National Cerebral and Cardiovascular Center, Japan*

The characteristics of patients with acute coronary syndrome (ACS) in Japan are fundamentally different from those from the United States and European countries, as revealed by previous studies. In Japan, aging is progressing more rapidly than other countries. And thus, it is known that the mean age of patients with ACS who undergo percutaneous coronary intervention (PCI) in Japan is also higher compared to the United States. Further understanding of the proper usage for antiplatelet and anticoagulant agents has become a crucial issue, especially in the medical treatment of ACS. In the past several years, various antiplatelet agents were introduced to the Japanese population that has a higher bleeding risk than the Western populations. Similar to antiplatelet and anticoagulant agents, β-blockers and statins have demonstrated differences in the Japanese population. "Japanese Circulation Society (JCS) 2018 guideline on diagnosis and treatment of ACS" has been recently updated and published in the official journal of Japanese Circulation Society (Kimura K, et al. Circ J. 2019 Apr 25;83(5):1085-1196) and will be introduced in KSC 2019.

**Myocardial Infarction 1**
**Joint Collaboration for Asian AMI Guideline**
›› Friday, Oct 18, 08:40-10:10 AM / Walker 2

*Continued from page 4*

geographic barriers for many patients, hybrid and "home-based" CR programs are also being developed. More studies are also needed to evaluate the utility of CR in patients after valve surgery, as well as in HF patients with preserved ejection fraction (HFpEF).

**Healthcare Policy: Special Lecture**
**Comprehensive Cardiac Rehabilitation**
›› Friday, Oct 18, 12:00-13:00 PM / Art

# Cross Specialty: Nephrology and Cardiology

## Contrast Induced Nephropathy: Nephrologist's Case and Review

*Eun Sil Koh, MD, PhD*
*The Catholic University of Korea Yeouido St. Mary's Hospital, Korea*

As contrast-enhanced radiologic imaging has become essential in diagnosis, the incidence of contrast related complications has been increasing. Contrast induced nephropathy (CIN) is one of those contrast-related complications and is defined as an increase in serum creatinine beginning 1–3 days after an intravascular contrast dose that is not attributable to any other cause. The plasma creatinine component of this definition has reasonable sensitivity. However, its specificity is poor because plasma creatinine concentration fluctuates by fluid shifts and effects of medication. Since other factors can precipitate acute kidney injury (AKI) after exposure to contrast agents, the terminology of 'contrast-associated AKI' has gained favor (**Figure 1**). Contrast-associated AKI is considered as a marker of an increased risk of serious adverse outcomes rather than a mediator of such outcomes. A previous study showed that although small postsurgical elevations in plasma creatinine levels were associated with increased 30-day mortality, small decrements in plasma creatinine levels (≤0.5 mg/dL) were also associated with increased mortality. Contrast-associated AKI is also influenced by the patient- and procedure-related factors. Pre-existing chronic kidney disease (CKD) is a powerful patient-related risk factor. Although diabetes mellitus is the main risk factor, the previous study showed that diabetes mellitus amplified susceptibility in patients with underlying CKD. As compared with the high-osmolality contrast agents, low-osmolality and iso–osmolality agents are associated with a lower risk of AKI. The use of contrast agents at a high volume or repeated administration has been shown to be associated with an increased risk. The prevention of contrast-associated AKI has focused mainly on the use of renal replacement therapies, pharmaceutical agents, and intravenous crystalloid. The benefits of prophylactic renal replacement therapy and of most pharmaceutical agents – such as acetylcysteine and statin – have not been proved with the provision of periprocedural intravascular volume expansion as the primary intervention to reduce the risk.

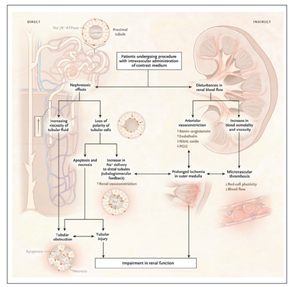



**Figure 1.** Proposed mechanisms of contrast-associated AKI (Adapted from Mehran R, et al. N Engl J Med 2019;380:2146)

Although the risk of contrast-induced AKI may be slightly higher in patients with moderate renal dysfunction (eGFR <45 mL/min or serum creatinine >2 mg/dL), the overall risk is still very low and contrast-enhanced imaging should not be denied. In patients with eGFR <30 mL/min, it may be plausible to minimize the overall use of contrast agents.

## Cardiorenal Syndrome: Nephrologist's Case and Review

*Tae Ik Chang, MD, PhD*
*National Health Insurance Service Ilsan Hospital, Korea*

Cardiorenal syndrome (CRS) includes disorders involving both the heart and kidney, in which functional impairment in one organ may induce functional dysfunction in the other organ acutely or chronically (**Figure 2**). Since the new classification of CRS with 5 subtypes has been proposed in the Consensus Conference by the Acute Dialysis Quality Group in 2008, much attention has been placed on elucidating the mechanisms of heart and kidney interactions and on describing the clinical consequences of each subtype. This classification essentially divides CRS into 2 main groups, cardiorenal and renocardiac CRS, based on the initiating disease of the organ (cardiac or renal). Both cardiorenal and renocardiac CRS are then divided into acute and chronic types according to the onset and duration of the underlying organ dysfunction. A remarkable interest has also been placed on overwhelming systemic conditions causing dysfunction of both organs, such as sepsis or diabetes (CRS type 5). Despite the in-depth understanding of pathophysiologic mechanisms, evidence-based advances in the past several decades have been relatively limited in terms of treatment options for CRS, in part because of the exclusion of patients with significant renal dysfunction from clinical trials, particularly those patients with acute CRS. More importantly, there is a clear need for cardiologists and nephrologists who are well-versed in the pathophysiology and clinical manifestations of CRS for optimal patient care of those patients at greatest need, in order to reduce the burden of serious sequelae, including the need for dialysis, permanent disability due to heart or kidney impairment, and death. In this regard, this session will comprise of brief summaries of CRS (definition, classification, pathophysiology, and treatment), clinical case presentations, and interactive panel discussions about issues related to the content being presented.

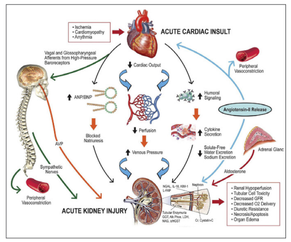



**Figure 2.** Pathophysiology of neurohumoral and inflammatory pathways involved in cardiorenal syndrome (Adapted from Rangaswami J, et al. Circulation 2019;139(16):e840-e878.)

**Cross Specialty: Nephrology and Cardiology**
**What Nephrologists Want to Say to Cardiologists**
›› Friday, Oct 18, 10:20-11:50 AM / Theatre

# Cross Specialty: Arrhythmia & Heart Failure

## Catheter ablation in patients with atrial fibrillation and heart failure

*Boyoung Joung, MD, PhD*
*Yonsei University Severance Hospital, Korea*

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population. AF increases the risk of mortality and morbidity resulting from stroke, congestive heart failure (HF), dementia, and impaired quality of life, which explains its enormous socioeconomic and healthcare implications. The prevalence of AF progressively increased by 2.10-fold from 0.73% in 2006 to 1.53% in 2015 in Korea. The prevalence of AF in the Korean population is expected to reach 5.81% (2,290,591 patients) by 2060. The prevalence of AF in HF increases with HF severity: based on New York Heart Association (NYHA) classification, 5% in class I to 50% in class IV HF. Together, AF and HF lead to atrial structural and electrical remodeling, and progression of paroxysmal to persistent AF, perpetuating a vicious cycle of impaired left ventricular (LV) filling, contractility, and cardiac output.

Catheter ablation for AF is superior to antiarrhythmic drugs in decreasing AF recurrences, prolongs the time in sinus rhythm, and improves the quality of life of patients. Recent randomized controlled trials including the CASTLE-AF study reported clinical improvements in mortality, HF hospitalizations, LV ejection fraction (LVEF), and quality of life in patients with HF with reduced ejection fraction (HFrEF) who had AF ablation (**Figure 1**). Unfortunately, complete success with catheter ablation (i.e., no recurrence with a single procedure and no need for antiarrhythmic drugs) is uncommon, and the rate of complications is not trivial. In the CABANA trial, catheter ablation for AF did not significantly reduce the primary composite endpoint of death, disabling stroke, serious bleeding, or cardiac arrest, compared with medical therapy. Therefore, the most recent guidelines support AF ablation with caution (class IIb recommendation) in patients with LV systolic dysfunction and HFrEF.

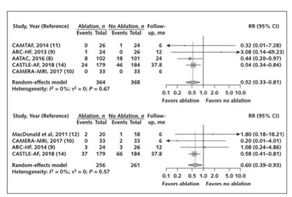



**Figure 1.** Forest plot of the decrease in all-cause mortality and HF hospitalization with catheter ablation compared with medical treatment for atrial fibrillation.

**Cross Specialty: Arrhythmia & Heart Failure**
**Catheter ablation in patients with atrial fibrillation and heart failure**
›› Friday, Oct 18, 15:40-17:10 PM / Theatre

# Women Heart Disease

## Gender Aspect in Sports Medicine

*Hack-Lyoung Kim, MD, PhD*
*Seoul National University Boramae Medical Center, Korea*

Regardless of age and gender, the number of people enjoying sports is increasing. In order to understand the difference between male and female in adaptation to sports and sport injuries, it's important to understand the difference in the musculoskeletal system between male and female.

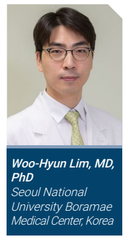
The role of sex hormones plays a pivotal role by influencing tissue composition and function. The bones in a female body mature earlier than those in the male body. As male bones continue to grow and develop longer, male skeletons generally have longer and thicker bones. On the other hand, a female body has a more rounded pelvis than that of a male to facilitate parturition.

Changes in ligaments and cartilages are also observed between the two sexes. More ligamentous laxity and severe cartilage loss, and increased muscle stiffness in females might explain the higher vulnerability to joint injuries. The striking post-pubertal increase in circulating testosterone in males provides a major physical advantage in sports by creating larger and stronger bones, as well as greater muscle mass and strength. Hence, on average, such differences hinder women to compete effectively against men in power-based or endurance-based sports. However, women tend to have a greater proportion of type 1 fibers and greater capillary density leading to hold of fatigue, and females usually exhibit less skeletal muscle fatigue relative to men during single-limb isometric contractions.

The lack of female hormones after menopause seems to be detrimental; muscle protein turnover is enhanced, and there is a net loss of muscle mass and a reduction in muscle function when women enter the postmenopausal state. In general, estrogen should be perceived as anabolic in relation to maintaining or even enhancing skeletal muscle function. Nevertheless, high levels of endogenously or exogenously administered estrogen in young women may disturb the protein balance in the tendon and ligaments in a non-beneficial direction in relation to sports injuries.

**Women Heart Disease 1**
**Exercise in Women**
›› Friday, Oct 18, 14:00-15:30 PM / Grand 4

## Sex Differences in Arrhythmia



*Woo-Hyun Lim, MD, PhD*
*Seoul National University Boramae Medical Center, Korea*

As with many diseases, there are sex-specific differences in arrhythmias. Whereas evidence for sex differences in ischemic heart disease and stroke have accumulated, the differences between women and men with cardiac arrhythmias have received less attention.

Women's heart size is smaller than that of men and the heart rate is faster. Due to the different electrophysiological characteristics, the effective refractory period (ERP) of sinus node and atrioventricular node in women is shorter than that of men, and the QT interval is longer in women. In addition, potential contributions of sex hormones should be considered. These differences lead to clinical differences between women and men with cardiac arrhythmias.

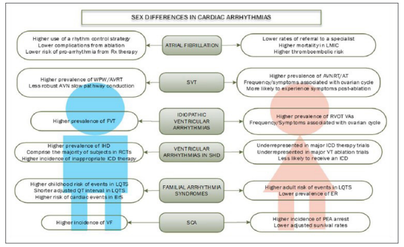



**Figure 1.** Overview of sex differences in cardiac arrhythmias (Adapted from Circ Arrhythm Electrophysiol. 2018;11:e005680.)

The incidence and prevalence of atrial fibrillation (AF) is higher in men worldwide. However, because women have a longer life expectancy than men and the prevalence of AF increases with age, the number of patients with AF is greater in women. Women with AF are more likely to experience more severe symptoms such as palpitations and anxiety, and are associated with higher rates of heart failure with preserved ejection fraction and valvular heart diseases, and lower quality of life scores than men. Women are also known to have a higher risk of stroke or systemic embolism, and women have one point on the $CHA_2DS_2$-VASc score. However, there is no significant difference in the risk of stroke between men and women according to the studies from Korea. When using new oral anticoagulants to prevent stroke, the effects and risks of bleeding are similar between men and women, but women are more likely to be prescribed with off-label low doses.

In terms of supraventricular tachycardia, the prevalence of atrioventricular nodal reentry tachycardia and atrial tachycardia is higher in women, while men have a higher prevalence of Wolff-Parkinson-White (WPW) syndrome and atrioventricular reentry tachycardia. Premenopausal women may have a cyclic trend of tachycardia throughout the menstrual cycle. Thus, if electrophysiology study and catheter ablation are planned, the menstrual cycle should be considered in scheduling the procedure.

Sudden cardiac arrest (SCA) has been reported to occur three times higher in men. If the left ventricular function is normal, there is no difference in SCA between men and women. However, in those with severe left ventricular dysfunction, men account for the majority of SCA. Pulseless electrical activity, on the other hand, is more frequent in women. In a meta-analysis of primary prevention implantable cardioverter defibrillators (ICD) trials, women had similar mortality compared with men while experiencing less ICD treatment for VT/VF (**Figure 1**).

Considering sex differences in the treatment of patients with cardiac arrhythmias may increase patient satisfaction and improve treatment outcomes. Future studies would provide stronger evidence regarding sex differences in cardiac arrhythmias.

**Women Heart Disease 2**
**Arrhythmia in Women**
›› Friday, Oct 18, 15:40-17:10 PM / Grand 4

# Lipid

## Lessons from Recent Outcome Trials of PCSK9 Inhibitors

*Sang-Hak Lee, MD, PhD*
*Yonsei University Severance Hospital, Korea*

Three outcome trials of PCSK9 inhibitors (FOURIER, SPIRE 1/2, and ODYSSEY Outcomes) showed that human monoclonal antibodies against PCSK9 can reduce cardiovascular risk in high-risk population. These trials have proven that further cardiovascular benefits can be obtained with acceptable safety by lowering low-density lipoprotein cholesterol (LDL-C) beyond current treatment target. The latest guidelines of lipid-lowering therapy introduced recommendation of PCSK9 inhibitors in some conditions. Because incremental reduction of cardiovascular risk in the trials was modest, identification and prioritizing of patient groups who are able to obtain the greatest benefit from these agents seems of paramount importance (**Figure 1**). Researchers are currently investigating LDL-C independent effect, siRNA-based PCSK9 modulation with enhanced adherence, and Lp(a) lowering capabilities of PCSK9 inhibitors. Some uncertain points remain to be addressed by further studies. Because only a small group of patients in the FOURIER and ODYSSEY Outcomes trials were on ezetimibe, PCSK9 inhibitor-induced benefit in a group receiving statin plus ezetimibe needs to be clarified. Longer-term safety is also pending. Finally, whether or not ethnic or individual variations in PCSK9 inhibitor response is large, and if so, the background for the variations can be another topic for further research.

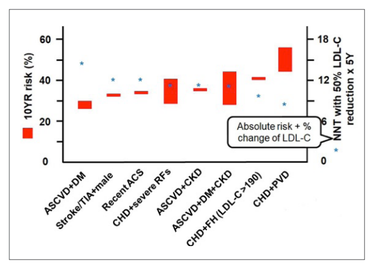



**Figure 1.** Risk stratification in ASCVD with additional risk factors: 10 year risk and NNT

**Lipid 1**
**Lesson Learned from Recent CV Outcome Clinical Trials Using Cardiometabolic Drugs**
›› Friday, Oct 18, 08:40-10:10 AM / Grand 4

# Featured Clinical Research 1

## Outcomes of Direct Oral Anticoagulants in Patients with Mitral Stenosis

*Ju Youn Kim, MD, PhD*
*The Catholic University of Korea Ujeongbu St. Mary's Hospital, Korea*

Patients with mitral stenosis and atrial fibrillation (AF) require anticoagulation for stroke prevention. Direct oral anticoagulants (DOACs) are effective in preventing thromboembolism among patients with AF. However, all studies on DOACs have excluded patients with moderate to severe mitral stenosis. Therefore, warfarin remains the only oral anticoagulant approved for patients with AF and moderate to severe mitral stenosis. In this study, we validated the efficacy of DOACs in patients with mitral stenosis.

Strokes or systemic embolisms and all-cause death rates were significantly lower in the DOAC group compared with the warfarin group. There was a non-significant difference in the rate of the incidence of intracranial hemorrhages between the DOAC group and the warfarin group. Thromboembolic events occurred at a rate of 2.22%/year in the DOAC group and 4.19%/year in the warfarin group (adjusted hazard ratio for DOAC: 0.28; 95% confidence interval: 0.18 to 0.45). Intracranial hemorrhage occurred in 0.49% of the DOAC group and 0.93% of the warfarin group (adjusted hazard ratio for DOAC: 0.53; 95% confidence interval: 0.22 to 1.26) (**Figure 1**).

This study revealed worthwhile exploratory data on the effectiveness of DOACs in patients with mitral stenosis and AF. In patients with AF accompanied by mitral stenosis, DOAC use is promising and hypothesis-generating in preventing thromboembolism. Our observation supports that DOAC use appears reasonable in patients with mitral stenosis and AF. Based on this consideration, a clinical trial evaluation of the superiority of DOACs in moderate to severe mitral stenosis would be justified. Our results need to be replicated in a randomized trial.

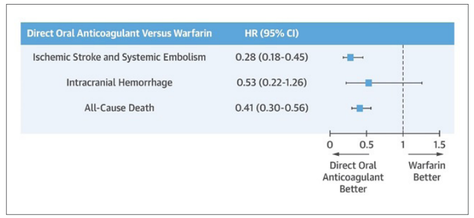



**Figure 1.** Mitral stenosis and atrial fibrillation for direct oral anticoagulant versus warfarin: Hazard ratios (Adapted from Kim JY, et al. J Am Coll Cardiol 2019;73(10):1123-1131.)

## Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy on Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention: The SMART-CHOICE Randomized Clinical Trial

*Joo-Yong Hahn, MD, PhD*
*Sungkyunkwan University Samsung Medical Center, Korea*

Data on P2Y12 inhibitor monotherapy after short-duration dual antiplatelet therapy (DAPT) in patients undergoing percutaneous coronary intervention (PCI) are limited. We studied whether P2Y12 inhibitor monotherapy after 3 months of DAPT is non-inferior to 12 months of DAPT in patients undergoing PCI in the SMART-CHOICE trial. It was an open-label, noninferiority, randomized study conducted in 33 hospitals in Korea and included 2,993 patients undergoing PCI with drug-eluting stents from March 2014 to July 2018. Patients were randomly assigned to receive aspirin plus a P2Y12 inhibitor for 3 months and thereafter P2Y12 inhibitor alone (n=1,495) or DAPT for 12 months (n=1,498). The primary endpoint was major adverse cardiac and cerebrovascular events (MACCE; a composite of all-cause death, myocardial infarction, or stroke) at 12 months after the index procedure. Secondary endpoints included the components of the primary endpoint and bleeding defined as Bleeding Academic Research Consortium type 2 to 5.

Among 2,993 patients who were randomized (mean age, 64 years; 795 women [26.6%]), 2,912 (97.3%) completed the trial. At 12 months, MACCE occurred in 42 patients in the P2Y12 inhibitor monotherapy group and in 36 patients in the DAPT group (2.9% vs 2.5%; difference, 0.4%; upper limit of 1-sided 95% CI, 1.3%; p=0.007 for noninferiority). There were no significant differences in all-cause death (21 [1.4%] vs 18 [1.2%]; HR, 1.18; 95% CI, 0.63–2.21; p=0.61), myocardial infarction (11 [0.8%] vs 17 [1.2%]; HR, 0.66; 95% CI, 0.31–1.40; p=0.28), or stroke (11 [0.8%] vs 5 [0.3%]; HR, 2.23; 95% CI, 0.78–6.43; p=0.14) between the two groups. The rate of bleeding was significantly lower in the P2Y12 inhibitor monotherapy group than in the DAPT group (2.0% vs 3.4%; HR, 0.58; 95% CI, 0.36–0.92; p=0.02) (**Figure 2**).

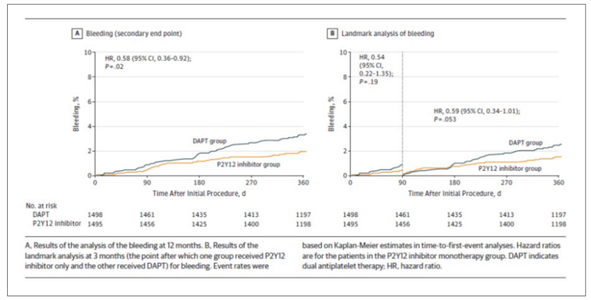



**Figure 2.** Time-to-event curves for the bleeding and landmark analysis at 3 months (Adapted from Hahn JY, et al. JAMA 2019;321(24):2428-2437.)

Among patients undergoing PCI, P2Y12 inhibitor monotherapy after 3 months of DAPT compared with prolonged DAPT resulted in non-inferior rates of MACCE. P2Y12 inhibitor monotherapy after the short-duration of DAPT is a novel antiplatelet strategy balancing ischemic and bleeding risk in patients undergoing PCI.

**Featured Clinical Research 1**
›› Friday, Oct 18, 14:00-15:30 PM / Theatre

# Imaging

## CMR as a Tool for Myocardial Tissue Characterization

*Vanessa Ferreira, MD*
*University of Oxford, UK*

The lecture by Dr. Vanessa Ferreira will review the clinical applications of cardiovascular magnetic resonance (CMR) as a multiparametric imaging modality for cardiac phenotyping, by using major techniques such as cine imaging, late gadolinium enhancement (LGE) imaging, stress perfusion imaging, and parametric T1/T2 extracellular volume (ECV) mapping. Cine imaging produces movie images of high spatial resolution for the evaluation of cardiac anatomy and function. LGE imaging permits non-invasive visualization of ischemic scars from myocardial infarction, which may be distinguished from non-ischemic etiologies based on LGE patterns, extent and distribution. CMR stress perfusion produces high-resolution images for the detection of regional inducible hypoperfusion to evaluate the functional significance of obstructive coronary artery disease, and the recent pixel-wise perfusion maps allow quantification of myocardial blood flow at rest and during stress, opening the doors for the non-invasive assessment of microvascular dysfunction.

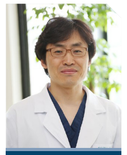
The lecture will cover clinical applications of T2 imaging as the first example of CMR mapping that achieved widespread clinical adoption, which is now routinely employed to assess myocardial iron loading and reducing cardiac death by 71% in patients with thalassemia. The European Society of Cardiology (ESC) Heart Failure Association Position Statement (November 2018) states that CMR Parametric Mapping is one of six Innovative imaging methods in assessing heart failure.

CMR is increasingly used in clinical practice and is expected to help diagnose and better manage patients with a variety of cardiac conditions as a "one-stop-shop" due to its multiparametric capabilities.

**Imaging 1**
**Multimodal Imaging Approach for Heart Failutre**
›› Friday, Oct 18, 08:40-10:10 AM / Pine

# Smart Health

## Clinical Application of Artificial Intelligence: True and False



*Seong Ho Park, MD, PhD*
*Ulsan University Asan Medical Center, Korea*

The use of artificial intelligence (AI) for medicine has recently drawn much attention due to the advances in machine learning techniques involving multiple layers of artificial neural networks trained on big data, i.e., deep learning. AI is a potentially transformative technology that can improve many aspects of healthcare. However, undoubtedly, AI has been creating much hype as well. In contrast with the hype of media and industry, few AI techniques are currently used in medical practice. Concerns are that many companies developing AI software tools for medical use are facing the risk of shutting down. For example, unlike what has been exposed to the public, IBM's Watson for Oncology is actually an example of failure by prematurely attempting clinical adoption. The MD Anderson Cancer Center tried to introduce Watson for Oncology in early 2017 but found problems and stopped the project after having spent $62 millions. Also, IBM laid off approximately up to 70 percent of staff in the corresponding business division in the first half of 2018.

It appears that the "short" hype phase has now been superseded by a sober understanding of the strengths and weaknesses of AI. Not only medical communities but also IT industry giants and AI leaders have started sharing and educating about the critical challenges for clinical adoption of AI technology. Notable problems include scarcity of AI-friendly medical big data and strong data dependency, limited generalizability, and low explainability of AI. With the increasing awareness of the pitfalls in applying AI to medicine, the importance of thorough clinical validation of AI is increasingly emphasized. The lack of appropriate clinical validation for AI algorithms, a phenomenon referred to as 'digital exceptionalism,' is a significant concern. Just as drugs and any other medical devices are required to pass a thorough validation of safety and efficacy before they can be used for patients, proper clinical validation is also critical for AI technology. One of the key points to consider when evaluating the accuracy of an AI algorithm is proper external validation. Proper external validation requires testing of the accuracy using datasets that are collected independently from the training dataset and adequately represent the target patient groups in well-defined real-world clinical scenarios (also, ideally collected from multiple institutions prospectively). The ultimate clinical validation of AI requires a demonstration of its value through a positive impact on patient outcome, beyond performance metrics, which would ideally require randomized trials.

In applying AI technology to patients, medical professionals should be in the driver's seat, not in the backseat. They are responsible for ensuring that AI becomes a technology beneficial for patient care by performing multiple roles, such as identifying proper cases for implementation, ensuring data quality, patient data protection/ethics, clinical validation, continued monitoring and health policy, as well as a provider of accurate, impartial information/education. These make the acquisition of sound knowledge and experience about AI a task of high importance for medical professionals.

**Smart Health**
**Medical Informatization and Heart Disease**
›› Friday, Oct 18, 14:00-15:30 PM / Cosmos

# JCS-KSC Joint Session: Basic Research

The main theme of the JCS-KSC Joint Session in basic research this year is "Roadmap for Cardiac Regeneration". Four distinguished speakers will present to attendees the achievements and current research trends in cardiac regeneration. This session will offer opportunities to learn from and interact with experts from Japan and Korea.

## Latrophilin-2, a G-protein Coupled Receptor: Functional Significance in Heart Development and Regeneration

*Hyun-Jai Cho, MD, PhD*
*Seoul National University Hospital, Korea*

Identification of lineage-specific markers is pivotal for understanding the developmental process and developing cell therapies. In today's lecture, Dr. Cho will report a new cardiac-specific cell surface marker, latrophilin 2 (Lphn2, Adgrl2), which is a G protein-coupled receptor (GPCR), and demonstrate its functional significance in cardiac progenitor cells (CPCs) and cardiomyocytes (CMCs) during in vitro differentiation from pluripotent stem cells (PSCs) and in vivo heart development.

Dr. Cho and his colleagues have demonstrated several novel findings as described below: They identified seven candidate genes and focused on the less-known GPCR, Lphn2, which is expressed on the cell surface. Lphn2 is expressed selectively on CPCs and CMCs during the differentiation of mouse iPSCs, and cell sorting with the anti-Lphn2 antibody facilitated the isolation of populations highly enriched for CPCs and CMCs. Moreover, in human cells (PSC-derived CPCs and CMCs) and human heart tissues, Lphn2 is a specific marker of cardio-myogenic cells; Lphn2 is necessary for cardiac development in vitro and in vivo. Their data suggest that Lphn2-expressing cells during development are cardiac muscle progenitors which are different from previously reported multipotent CPCs. The whole-mount immunostaining followed by the CLARITY technique showed that Lphn2 was expressed in the heart with three-dimensional and topological morphologies during the embryonic developmental stage. Using a Phospho Explorer Antibody Array covering nearly all known signaling pathways, they concluded that CDK5, Src, and P38MAPK are key downstream molecules of Lphn2. After they enriched PSC-derived Lphn2-positive cells on differentiation day 7 by FACS, they injected cells into the peri-infarct area of the mouse infarcted heart. Lphn2-positive cells showed several engrafted nodules, replaced the LV wall, and reduced the infarct size. The majority of cells expressed α-sarcomeric actinin as a cardiac muscle maker. Although Lphn2-negative cells also engrafted into the peri-infarct area, they did not differentiate into cardiac lineage cells. Lphn2 is the major inducer of signaling for cardiac development, including that for expression of Gata4, Nkx2.5, and Tbx5 as the central transcription factors for mouse heart development. At the amino acid level, mouse Lphn2 is highly homologous to the human protein (95.8% identical amino acid residues).

In summary, Dr. Cho and his colleagues demonstrated that Lphn2 is a functionally significant cell-surface marker for cardiac development, which uniquely marks cardiac muscle progenitor cells. The specific expression pattern of Lphn2 in PSC-derived cardiac lineage cells as well as in heart tissues of mouse embryos and of adult mice and humans suggests that this receptor plays a pivotal and functional role in all strata of the cardiomyogenic lineage, as early as the precursor stage of heart development. As Dr. Cho explains, "These findings provide a valuable tool to identify CPCs and CMCs from PSCs as well as novel insights into cardiac development".

## Engineering of Bioartificial Heart - Next Step for Cardiac Regeneration?

*Jong-Kook Lee, MD, PhD*
*Osaka University, Japan*

Induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) have been considered as promising cell sources for regeneration therapy, while disease-specific iPS-CMs have been utilized for disease modeling/drug discovery research for intractable heart diseases.

In most cases, iPS-CMs were arranged and analyzed as single cells or two-(2D)/three-dimensional (3D) tissues regardless of native anatomical structures. Although these tissues have recapitulated patients' phenotypes to a certain extent, there still exists a strong demand to regenerate 3D cardiac tissues physiologically- and anatomically-comparable to native hearts.

To elucidate the points, Dr. Lee engineered human-iPS-CM based atrial tissues mimicking the native anatomy of "pulmonary veins-left atrium junctions". As a result, the anatomy-based platforms successfully demonstrated characteristic atrial arrhythmogenic phenotypes.

Dr. Lee and his colleagues also attempted to achieve the engineering of "organ-like" 3D cardiac tissues using decellularized extracellular matrices (dECM). As a result, they have successfully constructed the dECM–based 3D-engineered hearts showing spontaneous beatings as a "whole organ" and demonstrated well-organized dynamic excitation-propagation using live cell/tissue imaging, although "the hearts" also demonstrated arrhythmogenic properties such as unsynchronized and disorganized conduction.

In today's lecture for introducing recent progress in the engineering of 3D cardiac tissues, Dr. Lee will discuss prospects and problems of engineering "Bioartificial Heart".

**JCS-KSC Joint Session: Basic Research**
**Roadmap for Cardiac Regeneration**
›› Friday, Oct 18, 14:00-15:30 PM / Calla

# Basic Research

## IntraVital Microscopy (IVM) for In Vivo Live Cell Imaging in Cardiovascular Diseases

***Pilhan Kim, PhD***
*Korea Advanced Institute of Science and Technology (KAIST), Korea*

Intravital microscopy enables dynamic 3D cellular-level imaging of various biological processes in a living animal in vivo. This unique capability allows scientists to directly verify a hypothesis based on data collected in ex vivo or artificial in vitro environments in a natural and physiological in vivo microenvironment at the cellular level. So far it has been utilized to directly image gene expression, protein activity, drug delivery, cell trafficking, cell-cell interaction, and physiological response to external stimuli in a live animal in vivo, which have provided unprecedented insights that were impossible to obtain with conventional static 2D observation ex vivo or in vitro.


**Figure 1.** Intravital imaging of the heart

In today's talk, Dr. Kim will describe a custom-built integrative intravital microscopy system capable of real-time sub-micron resolution multi-color fluorescence imaging of live animal model in vivo. The custom imaging system has been extensively optimized for in vivo cellular-level imaging of various internal organs of animal models for human diseases. Intravital microscopic imaging of the heart in a live anesthetized Prox1-GFP mouse was accomplished by utilizing a micro-suction assisted stabilized thoracic organ imaging window, which clearly showed lymphatic vessels (GFP) and capillaries (CD31), as shown in **Figure 1**. He will also introduce intravital microscopic imaging of various organs including lung, liver, spleen, pancreas, kidney, small intestine, colon, retina, lymph node, and bone marrow. Subsequently, recent studies utilizing the real-time intravital imaging technique to investigate dynamic cellular-level pathophysiology of various human diseases will be introduced.

**Basic Research 1**
**Recent Updates in Basic Cardiovascular Research**
›› Friday, Oct 18, 08:40-10:10 AM / Calla

## 3D Printed Complex Tissue Construct Using Stem Cell-laden Decellularized Extracellular Matrix Bioinks for Cardiac Repair

***Hun-Jun Park, MD, PhD***
*The Catholic University of Korea Seoul St. Mary's Hospital, Korea*

Myocardial infarction (MI) is a major contributor to cardiovascular disease, and it is the leading cause of death in the world. There is a large need for a therapeutic method for the treatment of post-MI adverse ventricular remodeling. Stem cell therapy is undergoing experimental and clinical trials in cardiology in order to limit the consequences of decreased contractile function and compliance of damaged ventricles following MI. However, a major challenge of the therapeutic use of stem cells for cardiac repair is poor cell engraftment in vivo after transplantation.

3D cell printing technology can regenerate tissue architecture similar to the cardiac niche by depositing various cells with a printable hydrogel called bioinks, which have greatly enhanced the versatility of 3D tissue/organ printing constructs. In today's talk, Dr. Park will present the results from his study about 3D cardiac patch using a bioinks composed of heart decellularized extracellular matrix (hdECM), embedded by cardiac progenitor cell (CPC) for cardiac muscle tissue and mesenchymal stem cells (MSC) with vascular endothelial growth factor (VEGF) for vascular tissue (**Figure 2**).

In this study, he demonstrated that 2% hdECM provided a favorable microenvironment for successful survival and maturation of CPCs compared to the same concentration of collagen. The hdECM bioink was also capable of printing various sizes of struts, and the stiffness of the printed hdECM structure was tuned around 10-20 kPa to match the native tissue environment. They developed 3 types of 3D printed cardiac patches using hdECM bioink, embedded by 1) hdECM only, 2) CPC (1x10^5), and 3) CPC/MSC (1x10^5) with VEGF and transplanted on the epicardium of infarcted rat heart. Serial echocardiography showed that three groups (hdECM, CPC and CPC/MSC) had higher ejection fractions than the control at 4 weeks. Interestingly, CPC/MSC group maintained cardiac functions for up to 8 weeks, although hdECM and CPC groups showed a dramatic reduction of cardiac functions during that time. Confocal microscope examination showed that human specific lamin A/C and CD31 positive cells in 3D printed cardiac patch migrated and formed cardiac precursor formation and vascular structures into the infarcted myocardium.

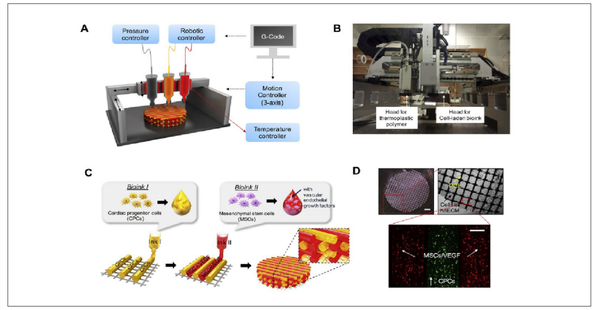



**Figure 2.** Schematic of pre-vascularized stem cell patch: (A) Illustration of the 3D cell printing system, and (B) macroscopic view of the printer; (C) Illustration of cardiac patch including multiple cell-laden bioinks and supporting PCL polymer; (D) Fabricated patch including the two types of cell-laden bioink and PCL supporting layer (Scale bar [left top], 1 mm; Scale bar [bottom], 200 mm)

This study demonstrated that a highly tunable 3D printed cardiac patch embedded by CPC/MSC enhances cell engraftment and cardiac function after post-MI. The results were published in the Biomaterials in 2017. This approach will ensure the achievement of a proper instructive cellular niche and facilitate cell retention, survival, and integration into the host heart tissue. Dr. Park explained, "Supported by relevant scientific background, the development of high-performance combinational cell therapy platforms using 3D bio-printing technology may constitute a new avenue and hope for the treatment of myocardial infarction".

**Basic Research 2**
**Tissue Engineering Technology Using Stem Cells for Cardiovascular Disease**
›› Friday, Oct 18, 10:20-11:50 AM / Calla



# Cardiometabolic Syndrome

## CV Benefit of SGLT2 Inhibitor: Cardiometabolic Mechanisms Beyond Its Hemodynamic Effect

***Sang-Man Jin, MD, PhD***
*Sungkyunkwan University Samsung Medical Center, Korea*

Recently, the results of the DECLARE-TIMI58 trial confirmed the benefit of SGLT2 inhibitors in the reduction of hospitalization rate for heart failure, even in patients with type 2 diabetes who were at high risk for cardiovascular (CV) events but did not have atherosclerotic cardiovascular disease (ASCVD) at baseline. All of the three major CV outcome trials of SGLT2 inhibitors showed consistent pattern that SGLT2 inhibitors have more robust and consistent effect on the prevention of heart failure and renal outcomes than on the atherosclerotic CV events.

Heart failure has been considered as a frequent, forgotten, and often fatal complication of diabetes. In the United Kingdom Prospective Diabetes Study (UKPDS), heart failure hospitalization incidence was similar to that of nonfatal myocardial infarction and stroke. Following myocardial infarction, people with diabetes have almost twice the rate of mortality and 3 times the rate of progression to congestive heart failure. This close link between heart failure and diabetes indicates that defects specific to the diabetic myocardium might contribute to greater mortality.

Although the diuretic and blood pressure-lowering hypothesis may in part explain the CV benefit of SGLT2 inhibitors, several hypotheses on cardiometabolic mechanism have been proposed. Importantly, as a compensation to the loss of glucose via glucosuria, SGLT2 inhibition causes a shift in the whole body fuel metabolism, resulting in increased free fatty acid and ketone levels. Ketone is a 'super fuel' for diabetic heart with metabolic inflexibility, in which inefficient fuel metabolism using free fatty acid is dominant due to insulin resistance. In addition, SGLT2 inhibition also exerts many anti-inflammatory effects (the anti-inflammatory effects hypothesis). In this talk, I will introduce the endocrinologists' view on the cardiometabolic mechanism of CV benefits from SGLT2 inhibitors beyond hemodynamic benefits.

**Cardiometabolic Syndrome 1**
**Hot Topic in Cardiometabolic Syndrome 1**
›› Friday, Oct 18, 08:40-10:10 AM / Art

## Out-of-Office Blood Pressure Measurement

***Il Suk Sohn, MD, PhD***
*Kyung Hee University Hospital at Gangdong, Korea*

For improving blood pressure (BP) control, accurate BP measurement is very important from the beginning. Accurate measurement and recording of BP are also essential to categorize BP level, assess BP-related cardiovascular risk, and guide management of hypertension. Recent guidelines for the management of hypertension recommend a standard protocol for office BP measurement. Although measurement of BP in office settings is relatively easy, it may not reflect an individual's "true" BP, for example, white coat hypertension (uncontrolled in office, but controlled in out-of-office) or masked hypertension (controlled in office, but uncontrolled in out-of-office).

Most hypertension guidelines recommend out-of-office BP measurement or self-monitoring of BP to assess the "true" BP in patients with hypertension not only in office but also in out-of-office and to confirm the diagnosis of hypertension and for titration of BP-lowering medication. Although ambulatory BP monitoring is generally accepted as the best out-of-office measurement method, self-monitoring or home BP monitoring (HBPM) is often a more practical approach in clinical practice, particularly for individuals taking antihypertensive medication. If self-monitoring is used, it is important to ensure that the BP measurement device used has been validated with an internationally accepted protocol and the results have been published in a peer-reviewed journal. There are some important evidence that have proven the predictive role of HBPM, which includes several observational studies conducted among community-based and clinic-based populations. In addition, there is now a large body of empirical evidence indicating better BP control with HBPM compared to usual care.

**Cardiometabolic Syndrome 2**
**Hot Topic in Cardiometabolic Syndrome 2**
›› Friday, Oct 18, 10:20-11:50 AM / Art


**11:00-11:30 New Frontiers in Cardiology 1**

Interviewer : Kee Sik Kim, Seung Woo Park
Interviewee : Achi Ludomirsky, Hyun Ho Park, Young Hak Kim, Kyung Woo Park

**12:00-12:30 Cross Specialty: Nephrology & Cardiology**

Interviewer: Beomsun Choi, Yangsoo Jang
Interviewee: Hyun-Jai Cho, Tae Ik Chang, In-Cheol Kim, Hyosang Kim

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# 2020
# 춘계심혈관 통합학술대회

2020 Annual Spring Scientific Conference of the KSC with Affiliated Cardiac Societies

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